Harmonization of Issues Involving Pesticide Exposure Assessment in North America

By

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(The Opinions are those of the author and not necessarily those of the Department or of the Agency.)

ABSTRACT

Harmonization of Issues Involving Pesticide Exposure Assessment in North America. John H. Ross, Department of Pesticide Regulation, Cal/EPA, Sacramento, CA 95814

Regulatory harmonization is a concept that has been popularized by the need of the Organisation for Economic Common Development (OECD) members to produce common requirements to encourage free trade. More recently, it has become a virtual necessity in North America for the same reasons. Additionally, downsizing of regulatory agencies necessitates greater efficiency, and exchangeability of review documents between agencies facilitates that goal. Scientists in the agencies regulating pesticides in North America (Canada; Health Canada, the United States; U.S. EPA, and California; Cal/EPA) have previously participated in the development of exposure monitoring protocols with scientists from member countries of OECD. More recently, the North American agencies have agreed to mutually consider nine issues (one agency has lead responsibility for three issues each). Many of the issues deal with the justification of default exposure values that are used in the absence of data specific to a particular situation. The exposure reduction offered by one layer of clothing, models to estimate indoor residential pesticide exposure, duration of exposure monitoring replicates, default physiologic factors, typical workday for various crops, and the decision not to require inhalation exposure monitoring or toxicology studies based upon low inhalation exposure potential are all areas under current consideration. The goal in each case is to develop a consensus position that can be endorsed by all agencies in North America. Time frames for producing draft issue documents for exchange between the agencies is late spring of 1996.

IMPLEMENTATION PLAN

The harmonization project described in this poster was solicited by the Office Director, Office of Pesticide Programs (OPP), U.S. Environmental Protection Agency (U.S. EPA) and the Executive Director of the Pest Management Regulatory Agency of Health Canada. It addresses an ongoing dialogue on occupational and residential exposure issues among representatives of U.S. EPA, Health Canada's Pest Management Regulatory Agency and the California Environmental Protection Agency's Department of Pesticide Regulation. Lead representatives in these agencies are: John Donahue, Branch Chief, and John Ross, Senior Toxicologist, of the Worker Health & Safety Branch, Department of Pesticide Regulation, California Environmental Protection Agency; John Worgan, Head, Occupational and Bystander Exposure Section, Pest Management Regulatory Agency, Health Canada; and Larry Dorsey, Branch Chief, Occupational and Residential Exposure Branch, Health Effects Division, OPP, U.S. EPA. Dialogue has occurred via conference calls and discussion at meetings mutually attended by the above representatives and their staff.

The goal of these efforts is to harmonize the assumptions and data analysis for worker and residential exposure assessments so that pesticide exposure reviews and work can be shared among all jurisdictions. This work expands on the past successful harmonization activities including the development of the draft OECD Occupational Exposure Assessment Guidelines and the Pesticide Handlers Exposure Database (PHED).

This poster is organized to include the following: an administrative workplan that provides an overview of the main issues, a separate section on each issue containing a summary of the issue or the purpose of the harmonization efforts; identification of the lead agency; and, delineation of objective milestones and target dates for each issue.

ADMINISTRATION WORKPLAN FOR HARMONIZATION ISSUES

The administrative workplan provides a global overview of the harmonization activities and identifies the expected completion date for each of the harmonization issues. While the completion date for some of these activities is not anticipated until 1997, individual milestones will be achieved prior to this time and will promote harmonization. Monthly conference calls will be held between the leads and other staff to track progress on all issues.

SUMMARY OF MAJOR ISSUES:

a) Protection Factors Provided by Clothing, etc.
February, 1996

b) Models for Indoor Residential Exposure:
April, 1997

c) Antimicrobial Exposure Database:
November, 1995

d) Exposure Duration of Monitoring Replicates:
April, 1996

e) Guidelines for Use of PHED:
May, 1996

f) Toxicology Triggers for Risk Assessment:
April, 1996

g) Standard Physiologic Reference Values:
February, 1996

h) Inhalation Exposure Waivers:
July, 1996

i) Typical Work Days for Various Crops:
February, 1997

j) Propose Post Application Exposure Guidelines to OECD[1]:
February, 1997

k) Develop *in vitro* Dermal Absorption Guidelines[1]:
April, 1996

1. Issues j and k are currently under development and not available

ISSUE: Protection Factors
LEAD AGENCY: U.S. EPA

PURPOSE/ PROBLEM: The purpose initially, is to utilize PHED data to evaluate the reduction of dermal exposure (resulting from mixing/loading and applying pesticides) to pesticides provided by one layer of clothing. All applicable paired observations, i.e., deposition outside clothing versus deposition inside one layer of clothing, will be compared. Further, paired observations will be grouped according to body region, i.e., forearms, upper arms, thighs, etc., and analyzed. Additional factors may be assessed in the future. Also, any protection factors currently being used by U.S. EPA, Health Canada and Cal/EPA-DPR will be exchanged among these groups for information, review and comment as appropriate.

MILESTONES:

1) Prepare draft of assumptions/methods. Evaluate preliminary statistical analysis and possibly recommend additional analysis. *Projected date: September, 1995.*

2) Request review and comment from Health Canada and CalEPA/DPR. *Projected date: October, 1995.*

3) Evaluate comments received and discuss with Health Canada and Cal/EPA-DPR the possibility of beginning to evaluate additional protection factors and possibly initiating analysis of additional factors. *Projected date: November, 1995*

4) Evaluate feasibility of preparing manuscript for possible publication. *Projected date: February, 1996.*

5) A list of protection factors currently used by U.S. EPA, Health Canada and Cal/EPA-DPR in assessing exposure to pesticides will be shared among the three jurisdictions for purposes of information, review and comment.
Projected date: February, 1996

ISSUE: Models for Indoor Residential Exposure
LEAD AGENCY: U.S. EPA

PURPOSE/ PROBLEM: To coordinate information on models for, and research on, indoor residential exposure.

MILESTONES:

1) Prepare chapter on Residential Indoor Exposure for the revised Subdivision K post application exposure guidelines. *Projected date: Draft chapter completedOctober, 1995.*

2) Request, review, and incorporate comments from Health Canada and Cal/EPA-DPR on draft chapter. *Projected date: In progress. Copies of draft chapter were sent to Health Canada and Cal/EPA-DPR for review in October, 1995.*

3) Evaluate Indoor Air Models used in other programs, states, countries. *Projected date: In progress.*

4) Monitor research being conducted by U.S. EPA Office of Research and Development in areas of indoor post application exposure (to include: surface residue sampling methodologies, contact and transfer methodologies); contact and transfer methodologies (transfer coefficients), and micro level activity monitoring methodologies. *Projected date: In progress.*

5) Evaluate results of research for updating Subdivision K. *Projected date: Fiscal year 1997.*

6) Evaluate "time in activity" databases and the U.S. EPA Exposure Factors Handbook as sources of information for indoor residential exposure models.
Projected date: June, 1996

ISSUE: Antimicrobial Database
LEAD AGENCY: U.S. EPA

PURPOSE/ PROBLEM: To coordinate the evaluation of existing exposure data related to antimicrobials, to determine the value of such data (i.e., "grade the data"), to compare existing independent databases (such as the Chemical Manufacturers Association [CMA] data) with data in PHED, to identify data gaps and to generate an issues paper on the topic of antimicrobial databases and the need for additional data.

MILESTONES:

1) Grade the studies in the CMA antimicrobial database, using input from Health Canada and Cal/EPA-DPR via teleconference and use of their existing review papers on the CMA database.
Projected date: September, 1995.

2) Compare the CMA data with any existing pertinent PHED data.
Projected date: October, 1995.

3) In conjunction with Health Canada and Cal/EPA-DPR, develop an issue paper addressing current data, including "grades" for the study data, PHED data as applicable, identify data gaps and delineate what the present policy on use of the data is for U.S. EPA, Health Canada and Cal/EPA-DPR.
Projected date: November, 1995.

ISSUE: Exposure Duration of Replicates
LEAD AGENCY: Health Canada

PURPOSE/ PROBLEM: The agencies currently have different philosophies with respect to duration of replicates in exposure studies (i.e., task vs. typical workday). This difference is frustrating to registrants attempting to conduct studies acceptable to all jurisdictions. Further this difference could limit work share opportunities between the agencies as submitted data is interpreted differently. Opportunities to harmonize will be investigated.

MILESTONES:

1) Identify staff contacts in U.S. EPA and Cal/EPA-DPR.
Projected date: Completed August, 1995.

2) Identify scope of issue.
Projected date: September, 1995.

3) Teleconference with staff contacts to identify: a) existing definitions and rationales; b) advantages and limitations of each approach; c) internal documentation & relevant references available.
Projected date: October, 1995.

4) Research outstanding issues.
Projected date: December, 1995.

5) Develop draft document and circulate it internally and externally to staff contacts.
Projected date: March, 1996.

6) Finalize Document.
Projected date: April, 1996.

ISSUE: Guidelines for Use of PHED
LEAD AGENCY: Health Canada

PURPOSE/ PROBLEM: Differences in analysis of PHED data and in the criteria for determining the acceptability of PHED data need to be identified. These differences could limit work share opportunities as submitted data may be interpreted differently. With a focus on issues related to harmonization, the possibility of obtaining consistency in the interpretaion of PHED data will be investigated.

MILESTONES:

1) Review available PHED assessments to confirm issues.
Projected date: November, 1995.

2) For major use scenarios, create list of body parts necessary for "whole body" data set method of analysis.
Projected date: September, 1995.

3) Review and discuss subsetting issues.
Projected date: November, 1995.

4) Resolve issues related to replicate duration and length.
Projected date: January, 1996.

5) Develop draft position paper and circulate internally and externally. *Projected date: February, 1996.*

6) Prepare final report. *Projected date: May, 1996.*

ISSUE: Toxicology Triggers for Risk Assessment
LEAD AGENCY: Health Canada

PURPOSE/ PROBLEM: The use of different toxicology triggers to request an exposure study is one area of difference between our agencies. This can lead to differences between the agencies as to whether exposure data is required.

MILESTONES:

1) Identify staff contact person from each agency.
Projected date: Completed August, 1995.

2) Conference call with staff contacts to discuss: a) existing policies and rationales; b) advantages and limitations of each approach; c) staff to provide all relevant information pertaining to this issue from U.S. EPA and Cal/EPA-DPR (e.g., Guidance Document and Process Statement for Less Than Lifetime Hazard Assessment, Toxicology Endpoint Selection Documents).
Projected date: September, 1995.

3)Prepare draft Position Document and distribute for comments.
Projected date: January, 1996.

4) Schedule conference call to discuss comments.
Projected date: February, 1996.

5) Incorporate comments.
Projected date: March, 1996.

6) Prepare final version of Position Document.
Projected date: April, 1996.

ISSUE: Standard Reference Values
LEAD AGENCY: Cal/EPA-DPR

PURPOSE/ PROBLEM: Each agency uses different default values for physiologic factors (such as body weight, surface area, and respiration rate) in their exposure assessment. Individually the differences in any given default are relatively small. However, since the factors are multiplicative, the differences in calculated exposure starting with the same pesticide concentrations in dosimetry matrices can be several fold. The goal of this task is to provide the justification for a fixed set of physiologic defaults which are consistent between agencies conducting exposure assessment.

MILESTONES:

1) Review and comment on the most recent revision of the U.S. EPA Exposure Factors Handbook and Health Canada's Standard Reference Value documents and make suggestions for any additional reference sources of physiologic factors.
Projected date: October, 1995.

2) Draft a proposal for review to use the values in the appropriate standard reference volumes at a fixed percentile of the population distribution for all physiologic factors and support that proposal with examples.
Projected date: November, 1995.

3) Propose sources of other physiologic factors not in the U.S. EPA Exposure Factors Handbook and suggest standard default values for review. *Projected date:December, 1995.*

4) Draft consensus issue paper incorporating agreements on default physiologic factors to be used by all agencies.
Projected date: February, 1996.

ISSUE: Inhalation Exposure Waivers
LEAD AGENCY: Cal/EPA-DPR

PURPOSE/ PROBLEM: It is well known that unless a pesticide has a vapor pressure approaching that of a fumigant, that inhalation exposure is only a small fraction of dermal exposure. But is it reasonable to not require inhalation studies or inhalation exposure monitoring on the basis that the physicochemical properties of the pesticide preclude significant exposure? Requiring unneeded exposure monitoring or toxicology is wasteful of resources for both generating the data and for reviewing it.

MILESTONES:

1) Identify current policies and their basis in each Agency. *Projected date: October, 1995.*

2) Estimate inhalation exposure for eight hours based on light work inhalation rate and a saturated atmosphere at vapor pressures of 10^{-5} -10^{0} millimeters of mercury by decade. *Projected date: October, 1995.*

3) Identify ambient air concentration that would produce 10^{-5} excess risk of oncogenicity if an individual were exposed for 8 hr/day, 200 days/yr for 40 yr if Q* were 1 $(mg/kg/day)^{-1}$. Identify ambient air concentration that would produce MOE (MOS in Canada and Calif.) of 100 from a NOEL of 1 mg/kg. *Projected date: November, 1995.*

4) Draft a proposal for interagency review recommending vapor pressure or mass median diameter of particles cutoffs for which inhalation toxicology or exposure monitoring need not be conducted. *Projected date: February, 1996.*

ISSUE: Typical Work Days for Various Crops
LEAD AGENCY: CalEPA/DPR

PURPOSE/ PROBLEM: Currently each agency assumes that the work day is approximately 8 hours. In reality exposure time varies as a function of work task. Number of hours worked is critical for calculating reentry worker exposure, while number of acres treated per day is a better measure of work day for pesticide handlers.

MILESTONES:

1) Establish sources of compiled data of typical work days for reentry workers and pesticide handlers.
Projected date: October, 1995.

2) Make proposal for estimated minimum number of reentry work tasks to characterize scope of workforce based on major labor-intensive crops.
Projected date: November, 1995.

3) Make proposal for database for handlers based on major types of application equipment and crops.
Projected date: December, 1995.

4) Determine the limiting factors that influence "work day." What factors limit the number of work days per year and work years in a lifetime a worker will handle agricultural pesticides?
Projected date: January, 1996.

5) Develop working database format skeleton of reentry worker typical work day. Issue draft of consensus paper for standard values used in exposure assessment to quantify daily, annual and lifetime exposure.
Projected date: March, 1996.